A self-limiting switch based on translational control regulates the transition from proliferation to differentiation in an adult stem cell lineage.

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Public Summary:
This manuscript reports the mechanism by which a fundamental transition of adult stem cells, from proliferation to differentiation, is regulated. The mechanism is unique but conserved across species, devlopmentally regulated and dependent on translation.

Scientific Abstract:
In adult stem cell lineages, progenitor cells commonly undergo mitotic transit amplifying (TA) divisions before terminal differentiation, allowing production of many differentiated progeny per stem cell division. Mechanisms that limit TA divisions and trigger the switch to differentiation may protect against cancer by preventing accumulation of oncogenic mutations in the proliferating population. Here we show that the switch from TA proliferation to differentiation in the Drosophila male germline stem cell lineage is mediated by translational control. The TRIM-NHL tumor suppressor homolog Mei-P26 facilitates accumulation of the differentiation regulator Bam in TA cells. In turn, Bam and its partner Bgcn bind the mei-P26 3' untranslated region and repress translation of mei-P26 in late TA cells. Thus, germ cells progress through distinct, sequential regulatory states, from Mei-P26 on/Bam off to Bam on/Mei-P26 off. TRIM-NHL homologs across species facilitate the switch from proliferation to differentiation, suggesting a conserved developmentally programmed tumor suppressor mechanism.